Departement für Nutztiere
Klinik für Reproduktionsmedizin
Abteilung für Kleintierreproduktion
der Vetsuisse-Fakultät Universität Zürich

Direktor: Prof. Dr. med. vet. Heiner Bollwein
Abteilungsleiterin: Prof. Dr. med. vet. Iris Margaret Reichler

Do prevalence rates and severity of acquired urinary incontinence differ between dogs spayed by laparoscopy or laparotomy? Comparing apples with apples with a matched pair cohort study

Inaugural-Dissertation

zur Erlangung der Doktorwürde der
Vetsuisse-Fakultät Universität Zürich

vorgelegt von

Katharina-Marie Lutz

Tierärztin
aus München, Deutschland

genehmigt auf Antrag von

Prof. Dr. med. vet. Iris Margaret Reichler, Referentin

2019

Für meine Eltern

Inhaltsverzeichnis

Vetsuisse Faculty University of Zurich (2019)

Katharina-Marie Lutz

Clinic of Reproductive Medicine, Small Animal Reproduction Unit
mwunder@vetclinics.uzh.ch

Do prevalence rates and severity of acquired urinary incontinence differ between dogs spayed by laparoscopy or laparotomy? Comparing apples with apples with a matched pair cohort study

Summary

Prevalence rates and severity of acquired urinary incontinence (AUI) between dogs spayed by laparoscopic and laparotomic approaches were compared using a retrospective matched-pair cohort study. A total of 1285 privately owned dogs spayed > 5 years previously were included in the study. Laparoscopically spayed dogs were matched with dogs spayed traditionally by laparotomy. Matching variables were breed, bodyweight, age at spaying, time of spaying in relation to the onset of puberty, time interval since spaying and age. In 400 matched paired dogs, the outcome of AUI was assessed using an owner questionnaire. A conditional logistic regression for matched pairs was performed on the data of 308 dogs. Out of 308 dogs, 30 and 29 dogs spayed by laparotomy and laparoscopy, respectively, were affected by AUI. The identified risk factors for AUI were age and time interval since spaying. The surgical approach, i.e., laparoscopy or laparotomy, was neither revealed as a risk factor nor did it influence the severity of AUI.
Nearly every fifth dog spayed by laparotomy or by laparoscopy was affected by AUI. Consequently, owners of dogs with a predisposition for AUI must be counseled about this risk when they present their dogs for spaying, regardless of surgical approach chosen.

Keywords: urinary incontinence, laparoscopy, spay, dog

Vetsuisse-Fakultät Universität Zürich (2019)

Katharina-Marie Lutz

Klinik für Reproduktionsmedizin, Abteilung für Kleintierreproduktion
mwunder@vetclinics.uzh.ch

Do prevalence rates and severity of acquired urinary incontinence differ between dogs spayed by laparoscopy or laparotomy? Comparing apples with apples with a matched pair cohort study

Zusammenfassung

Die Prävalenzraten und der Schweregrad der erworbenen Harninkontinenz (HI) wurde zwischen laparoskopisch und laparotomisch kastrierten Hündinnen in einer retrospektiven gepaarten Kohortenstudie verglichen. Insgesamt wurden 1285 Hündinnen in Privatbesitz, die > 5 Jahre kastriert waren, in die Studie eingeschlossen. Laparoskopisch kastrierte Hündinnen wurden mit konventionell, laparotomisch kastrierten Hündinnen gepaart. Paarungsvariablen waren Rasse, Körpergewicht, Alter bei Kastration, Zeitpunkt der Kastration in Relation zur Pubertät, Zeitintervall seit Kastration und Alter. Von 400 gepaarten Hunden wurde die Zielvariable HI mit Besitzerumfragen untersucht. Eine konditionelle logistische Regression wurde mit den Daten von 154 Hündinnenpaaren durchgeführt. Von diesen 308 Hündinnen waren 30 laparoskopisch und 29 laparotomisch kastrierte Hündinnen von HI betroffen. Identifizierte Risikofaktoren waren Alter und Zeitintervall seit Kastration. Der chirurgische Zugang, d.h. Laparoskopie oder Laparotomie, erwies sich weder als Risikofaktor noch beeinflusste er den Schweregrad der HI. Fast jede fünfte der untersuchten Hündinnen war gemäß ihrer Besitzer von HI betroffen. Somit müssen Besitzer von Hündinnen mit einer Prädisposition für HI über dieses Risiko aufgeklärt werden, wenn sie ihre Hunde für eine Kastration vorstellen, unabhängig davon ob ein laparotomischer oder laparoskopischer Zugang gewählt wird.

Schlüsselwörter: Harninkontinenz, Laparoskopie, Kastration, Hund

Do prevalence rates and severity of acquired urinary incontinence differ between dogs spayed by laparoscopy or laparotomy? Comparing apples with apples with a matched-pair cohort study

Katharina M. Lutz[1] med vet, Sonja Hartnack[2] Dr med vet, Diplomate ECVPH, Iris M. Reichler[1] Prof, Dr med vet

[1]Clinic of Reproductive Medicine, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland
[2]Section of Epidemiology, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland

Part of the results were presented at the 21st EVSSAR Congress, Venice, Italy, 23 June 2018

Corresponding author: Iris M. Reichler, Winterthurerstr. 260, CH-8057 Zurich, Switzerland, ireichler@vetclinics.uzh.ch

Abstract

Objective: To compare the prevalence rates and severity of acquired urinary incontinence (AUI) between dogs spayed by laparoscopic and laparotomic approaches.
Study Design: This was a retrospective matched-pair cohort study.
Animals: A total of 1285 privately owned dogs spayed > 5 years previously were included in the study.
Methods: Laparoscopically spayed dogs were matched with dogs spayed traditionally by laparotomy. Matching variables were breed, bodyweight, age at spaying, time of spaying in relation to the onset of puberty, time interval since spaying and age. In 400 matched paired dogs, the outcome of AUI was assessed using an owner questionnaire. A conditional logistic regression for matched pairs was performed on the data of 308 dogs.
Results: Out of 308 dogs, 30 and 29 dogs spayed by laparotomy and laparoscopy, respectively, were affected by AUI. The identified risk factors for AUI were age and time interval since spaying. The surgical approach, i.e., laparoscopy or laparotomy, was neither revealed as a risk factor nor did it influence the severity of AUI.
Conclusions: The risk of AUI after spaying is not influenced by the surgical approach, i.e., laparoscopy or laparotomy. Nearly every fifth dog spayed by laparotomy or by laparoscopy was affected by AUI. A relatively longer time interval since spaying and increased age of the dog increased the risk for AUI.
Clinical Significance: Owners of dogs with a predisposition for AUI must be counseled about this risk when they present their dogs for spaying, regardless of surgical approach chosen.

Introduction

Spaying is one of the most frequent surgeries performed in small animal practices. Dog owners should be counseled about the advantages and disadvantages of spaying as well about different surgical procedures, i.e., ovariectomy (OE) or ovariohysterectomy (OHE), and surgical approaches, e.g., laparoscopy or traditional laparotomy.

Acquired urinary incontinence (AUI) is a benign condition that can be treated successfully in the vast majority of cases,[1-3] but it may increase the likelihood of relinquishment as well as euthanasia.[4] The relationship between AUI and spaying was postulated for the first time more than half a century ago,[5] and its causality was shown in the 1980s.[6] Although the strength of this evidence was questioned by a systematic review of peer-reviewed original English journal articles,[7] recent results have confirmed this causal relationship.[4,8] Prevalence rates of AUI up to 20% have been reported; however, they vary tremendously among studies, most likely reflecting different demographic compositions.[4,6,9-22] Breed, size or bodyweight of the dog; obesity or body condition score (BCS); tail docking; urethra length; age of the dog; and the time of spaying in relation to the onset of puberty are considered potential risk factors of AUI.[1,4,9,11-13,15-17,19,20,22-28] For the different surgical procedures of spaying, i.e., OHE and OE, no differences were observed for the incidence of AUI.[27] Similarly, the risk for AUI did not differ between laparoscopic ovariectomized and laparoscopic-assisted ovariohysterectomized dogs.[22]

Laparoscopic spaying is becoming more popular.[29] Due to the smaller incisions needed, it is less invasive,[30] less painful[30-32] and therefore allows faster recovery time[33,34] compared with the traditional approach of laparotomy. The reported prevalence rates of AUI of 9%[22] and 15.4%[21] in dogs spayed laparoscopically are within the wide range reported in the literature for spaying using the traditional laparotomic approach.[4,6,9-20] However, comparing data from different populations without adjusting for different population-specific demographics may lead to bias in the interpretation of the results. Important confounders for AUI and the surgical approach are breed and bodyweight; large breeds have a higher risk for AUI[4,11,13,15-17,20,23-25] and are supposedly more likely to be spayed by laparoscopy.[31]

To investigate the hypothesis that the laparoscopic approach reduces the risk for AUI after spaying, a retrospective matched-pair cohort study was performed. We compared the prevalence rates and the severity of AUI between dogs spayed laparoscopically and dogs spayed by laparotomy (without distinguishing ovariectomized and ovariohysterectomized dogs) by controlling for confounders including breed, bodyweight, time of spaying in relation to the onset of puberty, age at time of spaying, time interval since spaying and age of the dog.

Materials and methods

Data collection

The medical records of dogs spayed between January 1999 and December 2012 were retrieved from two veterinary hospitals. The extracted data included owner information (name, address, phone number and email address if available); signalment and surgical information for each dog (date of birth, date of spaying, breed, bodyweight at time of spaying; the surgical approach of spaying, i.e., laparotomy or laparoscopy) and the name of the veterinary hospital. The surgical procedure, i.e., OE or OHE, was recorded and summarized under the term spayed. Data from 1285 dogs were stored on a spreadsheet (Microsoft® Excel 2011 for Mac) by the first author. Dogs were selected from the group of laparoscopically spayed dogs and matched with dogs spayed traditionally by laparotomy. Matching was performed at ratios of 1:1 to 1:4 according to breed or breed type, bodyweight, age at spaying, time of spaying in relation to the onset of puberty and time interval since spaying as well as the age of the dog. Mixed breed dogs were matched according to the breeds of their parents or, in cases of unknown pedigree, matched according to their bodyweight. The first author, who was blinded to the surgical approach data, contacted the owners of the selected dogs by phone or email and asked them to participate in a questionnaire-based survey investigating long-term effects of spaying.

The questionnaire included 18 questions, such as bodyweight in kilograms, BCS on a 9-point scale[35], which was assessed by the owner according to the instructions given by the questioner, and time of spaying in regard to the onset of puberty, i.e., before or after the first estrus. Furthermore, data on current health condition, medications and occurrence of AUI were collected. If AUI was a complaint, questions regarding its severity, i.e., the first occurrence and frequency of episodes per day and days per week, were asked. Additionally, the body position, i.e., lying, sitting and/or walking and waking state, i.e., while sleeping and/or awake, of the dog during urine leakage were asked. Information was also obtained from the owner about the presence of polyuria/polydipsia (PU/PD), concurrent use of medications at first occurrence of AUI and the clinical work-up for AUI, with special regard to urinalysis, urine bacterial culture and imaging results.

The time interval since spaying, which was calculated using the date of the questionnaire for dogs still alive and the date of death for deceased dogs, was at least 5 years. If urinary incontinence was reported, the dogs were included only if their first episode occurred after spaying and if they showed no PU/PD at the time of first occurrence. Furthermore, dogs with suspicion of urinary incontinence unrelated to spaying, e.g., with concurrent neurological signs, endocrine or metabolic diseases or receiving medication known to cause PU/PD, as well as dogs with behavioral micturition problems, in which urination occurs under voluntary control, were excluded from the final analysis. As soon as the questionnaires for both dogs of a matched-pair were completed, other possible matching partners were disregarded.

Statistical analyses

Statistical analysis was performed using SPSS (version 25; IBM Corp. Armonk, NY).

To assess the matching procedure, paired t-tests were applied to obtain the 95% confidence intervals (CIs) for the differences in the means of the continuous variables, i.e., bodyweight, BCS, age at spaying, time interval since spaying and age of the matched paired dogs. Range and/or mean ±standard deviation of these variables are presented for dogs spayed by laparoscopy, for dogs spayed by laparotomy as well as for all matched paired dogs.

For the severity of AUI, i.e., the time interval between spaying and the first occurrence of AUI, age at first occurrence of AUI, duration since the first occurrence as well as number of incontinence episodes per day and per week, the range and/or mean values ± standard deviations are given. The severity of AUI was compared between the groups of dogs spayed laparoscopically and by laparotomy using an unpaired t-test.

For the conditional logistic regression for matched pairs, the R program (2018, R Foundation for Statistical Computing, Vienna, Austria) was used. Continuous variables included in the analysis were bodyweight and BCS at the time the questionnaire was performed, age at spaying and time interval since spaying or observed age. As the variables time interval since spaying and age of the dog were interdependent but both of interest, two logistic regression analyses were performed. Factors included continence status, i.e., continent or incontinent, and the surgical approach, i.e., laparoscopy or laparotomy; the 95% CIs are given.

For all statistical tests, p-values below 0.05 were considered significant.

Results

Out of the total data set, 400 dogs were matched. However, once the questionnaires had been completed, 46 dogs did not meet the inclusion criteria; 26 dogs died within 5 years after spaying, 5 dogs presented the first episode of AUI before spaying, 11 dogs had PU/PD at the time of the first occurrence of AUI, one dog urinated in the house during a storm and 3 dogs had suspected neurological disease. All 46 dogs were excluded from the final analysis. Therefore, out of the remaining 354 dogs, 32 dogs spayed by laparotomy and 14 dogs spayed laparoscopically could not be matched to dogs of similar breed, bodyweight and time of spaying.

A total of 154 matched pairs of dogs spayed laparoscopically or by laparotomy were finally included in the analyses. Ninety-five matched pairs were purebred dogs of the same breed, 13 pairs consisted of purebred dogs paired with F1 generations of the same breed, 8 pairs were F1 offspring with one parent each belonging to the same breed, 12 pairs consisted of closely related purebred dogs, e.g., Labrador Retriever matched to Golden Retriever, and 26 pairs consisted of mixed breed dogs matched to dogs of similar bodyweights. Thirty-seven dog pairs were spayed before the onset of puberty, and 117 pairs were spayed after puberty. Additionally, the matched paired dogs were similar with regard to their bodyweight, BCS, age at spaying, time interval since spaying and age (Table 1). Their bodyweight varied between 4 and 70 kg (27.1±10.9) and their BCS varied between 1 and 8 (4.7±1.0). The dogs had been spayed between the ages of 0.2-8.5 (1.6±1.4) years. The time interval since spaying was 5.0 to 15.3 (8.7±2.6) years, and all dogs were between 5.5-18.7 (10.3±2.8) years of age.

AUI was described by the owners of 29 (18.8%) dogs spayed via laparotomy and 30 (19.5%) dogs spayed via laparoscopy. Of the purebred dogs with 4 or more representatives, the most commonly affected breeds were Doberman, Rhodesian Ridgeback and Great Dane, followed by Husky and Magyar Vizsla (Figure 1). The first episode of AUI was noted by the owners immediately or up to 13 (4.9±4.2) years after spaying. The dogs were between 6 months and 15 years old (6.5±4.5 years), when AUI was observed for the first time. AUI was noted since 4.6 (±3.8) years and occurred up to 7 (1.7±1.4) times daily, with a mean of 5.1 (±2.6) days per week. AUI was observed on a daily basis in 22 dogs, while 6 dogs presented AUI episodes less than once per week, and in 1 dog, it was noted only after swimming. Urine loss was mostly observed when the dogs were lying down but also during walking or sitting, e.g., 9 dogs experienced incontinence only during walking (Figure 2). Most of the dogs experienced incontinence only during sleep (n=21) or while sleeping and awake (n=21), while 12 dogs suffered from incontinence only when awake. For the remaining 5 incontinent dogs, this information could not be obtained.

The time interval between spaying and first occurrence of AUI as well as the time interval since the first occurrence of AUI did not differ between the dogs spayed by laparotomy or laparoscopy (p=0.198 and p= 0.469, respectively). Similarly, the daily and weekly occurrence of incontinence episodes were comparable between the dogs spayed by laparotomy or laparoscopy (p=0.255 and p=0.383, respectively).

Results of the conditional logistic regressions for matched pairs are shown in Table 2: The time interval since spaying and age but not the surgical approach, bodyweight, BCS, or age at spaying are revealed as risk factors for AUI.

Discussion

Within the last decade, laparoscopic spaying has become more popular.[29,33] We investigated if this less invasive approach compared to laparotomy reduces the risk of AUI, which is a side effect of spaying (Supporting Information Table). Some of the consistently reported risk factors, e.g., breed, tail docking and bodyweight, are not only closely related[23] but also may interfere with the chosen type of surgical approach. Risk assessment of AUI is further hindered because other risk factors such as time of spaying in relation to age or the onset of puberty are controversially discussed.[7-9,14,15,19,20,23,26] Additionally, the time of spaying and the type of surgical approach may interact to some extent with social, cultural or geographical differences. To accurately counsel owners on when and how to spay their dogs, scientific evidence is needed. In the past, it was shown that using the same approach but changing the surgical procedures, e.g., OE or OHE performed by laparotomy[12,13,16,17,20,25,27] or laparoscopy[22] or OHE with or without removal of the cervix,[9] did not influence the risk for AUI.

To answer the question of whether the surgical approach of spaying may impact the risk for AUI or, more precisely, if laparoscopic spaying reduces the risk for AUI, a matched-pair cohort study design was chosen. According to the CIs for the differences in the means, matching was successfully performed for the possible confounders, i.e., bodyweight, age at spaying, time interval since spaying and age. Comparing paired dogs, one spayed by laparoscopy and one spayed by laparotomy, which were matched for these confounders as well as for breed and the time of spaying with regard to the onset of puberty, clearly revealed that the surgical approach was not a risk factor for AUI; 30 (19.5%) laparoscopically spayed dogs and 29 (18.8%) dogs spayed by laparotomy developed AUI. Furthermore, the severity of AUI, e.g., the frequency and first occurrence, did not differ between affected dogs spayed using the laparoscopic or laparotomic approach. However, by using continence scoring systems addressing the associated amount of urine loss[36-39], the severity could have been assessed even more precisely. Still, according to the previously and the herein presented results, the invasiveness of the surgery, i.e., the surgical procedure[9,12,13,16,17,20,22,25,27] and the surgical approach, did not influence the risk for AUI. Therefore, the assumption that endocrine changes associated with spaying[14,40] are causative factors of AUI is further supported. Changes in collagen content;[41,42] the amount of glycosaminoglycan;[43] prostaglandin synthesis and its receptor expression;[44] COX-2 expression;[45] and changes in gonadotrophin releasing hormone (GNRH), follicle stimulating hormone (FSH) and luteinizing hormone (LH) secretion and receptor expression[14,46-49] are reported to occur after spaying. These factors may play a role in the pathophysiological mechanism of AUI. However, the exact role and relationship of these mechanisms have not been fully elucidated. The AUI prevalence rates of 18.8% and 19.5% in dogs spayed using the laparotomic or the laparoscopic approach reported herein are within the frequencies reported previously by our group,[16,20] but they are substantially higher than the rates reported by other investigators.[4,6,9-13,15,17-19,21,22] The widely varying prevalence rates (Supporting Information Table) are most likely reflective of different study designs and study populations.[4,50] If case definitions are relying on owner reports of AUI, the number of revealed cases might be increased due to incorrect case identification despite thorough questioning by phone by a veterinarian. Nine dogs with incontinence only experienced urine loss while walking were included according to the criteria of the study, although dogs with urethral sphincter mechanism incompetence (USMI), which is the most common form of AUI due to spaying, showed uncontrolled loss of urine mainly during resting.[16,51] AUI classification on the basis of the reports of owners cannot be equated to a medical diagnosis of AUI due to spaying. However, by including only veterinarians' diagnosis of USMI or solely the AUI cases responding to hormonal therapy, some milder cases that were not presented to a veterinarian or not treated may be missed.[23] Owners most likely ask for a veterinarian's advice if the hygienic or emotional aspects of AUI outweigh the expenditure of time and/or financial burden associated with bringing the dog to a veterinarian.[4]

Higher prevalence rates will also be observed with a longer period of observation. In the present study, increasing time interval since spaying and increasing age were the only risk factors revealed for AUI in the conditional logistic regression of matched pairs. The observed time interval since spaying, with a mean of 8.7 years, was considerably longer than that in previous studies[19,20] and most likely resulted in capturing more AUI cases. The first occurrence of AUI occurred up to 13 years after spaying, with a mean of 4.9 years, according to the owners in our study, while in previous studies, AUI occurred at a mean of 2 to 4 years after spaying.[11,15,16,20,40] Increased time intervals since spaying lead to increased odds of AUI, as previously established by results of our own group.[26] Moreover, an increasing risk for the development of AUI with progressing age has already been shown by studies relying on a veterinary diagnosis of AUI[4,9] or owner questionnaires.[23] The advanced age of dogs included in our study, with most dogs in their last stage of life,[52-55] resulted in an AUI prevalence rate just below 20%, which may closely reflect the lifetime risk for AUI.

Although the period of observation in the present study was considerably longer than those in two previous studies by our group,[14,16] the AUI prevalence rates were similar. This discrepancy might reflect the willingness of owners to participate in a scientific study if their dogs were affected by the condition investigated. While both previous studies examined and focused on the pathophysiology of AUI after spaying, the study presented here was promoted under the title "long-term effects of spaying", and AUI was not explicitly mentioned as a study subject.

Bodyweight was described as a risk factor for AUI in many studies,[1,4,11,13,15-17,20,23-26] but it was not a risk factor for AUI in the conditional logistic regression of matched pairs in the current study. This is not surprising, as matching was performed primarily for breed. In nearly two-thirds of all matched pairs, the paired dogs belonged to the same breed. Breed is a factor that clearly influences bodyweight.[4] Furthermore, bodyweight was also considered in the matching procedure. Previously, higher AUI rates in Boxers than in dogs belonging to other breeds but with a similar bodyweight were observed.[14] Breed affiliation seems to have a major impact on AUI, and most of the commonly affected breeds in our study, i.e., Doberman, Rhodesian Ridgeback and Great Dane, as well as most of the high-risk breeds mentioned in the literature[4,11,16,23,24] have a body weight above 15 kg. Nevertheless, within a breed, the risk for AUI is influenced by bodyweight, i.e., below-average bodyweight within a breed reduces the risk for AUI.[4] Bodyweight reflects the BCS and/or height. Obesity was discussed previously as a risk factor for AUI.[56] To differentiate between obesity and height, BCSs were included in our analysis. Similar to bodyweight, an evident impact of the BCS on AUI could not be shown. However, the BCS was assessed by the client following the instructions given by the first author performing the questionnaire. This may reduce the reliability of the BCS evaluation.

Similar to bodyweight and BCS, age at spaying and time of spaying in relation to the onset of puberty were previously discussed as risk factors for AUI[7-9,14,15,19,20,23,26] and therefore were also included as matching variables in the current study. Although we did not find an effect of timing of spaying on AUI, this could not be conclusively assessed because of the applied matching procedure.

A matched-pair cohort study is likely the most efficient way to control for potential risk factors, i.e., breed, time of spaying in relation to the onset of puberty, bodyweight, age at spaying, time interval since spaying and age in our study. However, matching reduces the variance in the matched variables and thereby the probability of detecting them as predictive factors. Although we attempted to carefully assess our matching process by paired t-tests and subsequent CIs of the differences in the means, it is still possible that we introduced bias into our data set. A randomized prospective experiment would be clearly advantageous but quite difficult to perform in a clinical setting within a reasonable time frame. We chose the matched-pair study design to clearly delineate the effect of the surgical approach on AUI by reducing the effect of possible confounders. According to our results, the hypothesis that dogs spayed laparoscopically have a lower prevalence rate or severity of AUI compared to dogs spayed by the laparotomic approach is rejected.

Ideally, for owner decision making with regard to reproduction control, veterinarians should counsel their clients individually and be aware of the advantages and disadvantages of spaying with regard to breed predispositions.[57-60] Furthermore, the benefits and risks of different surgical procedures and approaches for spaying must be addressed. Our findings show that one in five dogs exhibited AUI within a mean period of 4.9 years after being spayed by either laparotomy or laparoscopy. It is therefore important that owners of dogs with a predisposition for AUI receive advice on the risks, regardless of the approach used. Even though the reduced invasiveness of the laparoscopic approach allows faster recovery and less pain,[30-34] it does not seem to reduce the risk for AUI.

Acknowledgments

We are deeply grateful to the participating dog owners and the veterinary clinics.

Disclosure statement

The authors declare no conflicts of interest related to this report.

References

1. Byron JK, Taylor KH, Phillips GS, Stahl MS. Urethral Sphincter Mechanism Incompetence in 163 Neutered Female Dogs: Diagnosis, Treatment, and Relationship of Weight and Age at Neuter to Development of Disease. *J Vet Intern Med*. 2017;31(2):442-448.
2. Noel S, Claeys S, Hamaide A. Acquired urinary incontinence in the bitch: update and perspectives from human medicine. Part 2: The urethral component, pathophysiology and medical treatment. *Vet J*. 2010;186(1):18-24.
3. Reichler IM, Hubler M. Urinary incontinence in the bitch: an update. *Reprod Domest Animal*. 2014;49 Suppl 2:75-80.
4. O'Neill DG, Riddell A, Church DB, Owen L, Brodbelt DC, Hall JL. Urinary incontinence in bitches under primary veterinary care in England: prevalence and risk factors. *J Small Anim Pract*. 2017;58(12):685-693.
5. Joshua JO. The Spaying of Bitches. *Vet Rec*. 1965;77:642-646.
6. Thrusfield MV. Association between urinary incontinence and spaying in bitches. *Vet Rec*. 1985;116(26):695.
7. Beauvais W, Cardwell JM, Brodbelt DC. The effect of neutering on the risk of urinary incontinence in bitches - a systematic review. *J Small Anim Pract*. 2012;53(4):198-204.
8. Pegram C, O'Neill DG, Church DB, Hall J, Owen L, Brodbelt DC. Spaying and urinary incontinence in bitches under UK primary veterinary care: a case-control study. *J Small Anim Pract*. 2019.
9. Thrusfield MV, Holt PE, Muirhead RH. Acquired urinary incontinence in bitches: its incidence and relationship to neutering practices. *J Small Anim Pract*. 1998;39(12):559-566.
10. Brinkmann J. *Verhalten sich kastrierte Hunde anders als nicht kastrierte? Ergebnisse einer Besitzerbefragung*: Institut für Tierschutz und Verhalten, Tierärztliche Hochschule Hannover; 2015.
11. Holt PE, Thrusfield MV. Association in bitches between breed, size, neutering and docking, and acquired urinary incontinence due to incompetence of the urethral sphincter mechanism. *Vet Rec*. 1993;133(8):177-180.
12. Veronesi MC, Rota A, Battocchio M, Faustini M, Mollo A. Spaying-related urinary incontinence and oestrogen therapy in the bitch. *Acta Vet Hung*. 2009;57(1):171-182.
13. Okkens AC, Kooistra HS, Nickel RF. Comparison of long-term effects of ovariectomy versus ovariohysterectomy in bitches. *J Reprod Fertil Suppl*. 1997;51:227-231.
14. Reichler IM, Hung E, Jochle W, et al. FSH and LH plasma levels in bitches with differences in risk for urinary incontinence. *Theriogenology*. 2005;63(8):2164-2180.
15. Forsee KM, Davis GJ, Mouat EE, Salmeri KR, Bastian RP. Evaluation of the prevalence of urinary incontinence in spayed female dogs: 566 cases (2003-2008). *J Am Vet Med Assoc*. 2013;242(7):959-962.
16. Arnold S, Arnold P, Hubler M, Casal M, Rusch P. [Urinary incontinence in spayed female dogs: frequency and breed disposition]. *Schweiz Arch Tierheilkd*. 1989;131(5):259-263.
17. Angioletti A, De Francesco I, Vergottini M, Battocchio ML. Urinary incontinence after spaying in the bitch: incidence and oestrogen-therapy. *Vet Res Commun*. 2004;28 Suppl 1:153-155.
18. Krawiec DR. Diagnosis and Treatment of Acquired Canine Urinary-Incontinence. *Companion Animal Practice*. 1989;19(8-9):12-20.
19. Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in dogs. *J Am Vet Med Assoc*. 2004;224(3):380-387.
20. Stocklin-Gautschi NM, Hassig M, Reichler IM, Hubler M, Arnold S. The relationship of urinary incontinence to early spaying in bitches. *J Reprod Fertil Suppl*. 2001;57:233-236.

21. Binder C, Katic N, Aurich JE, Dupre G. Postoperative complications and owner assessment of single portal laparoscopic ovariectomy in dogs. *Vet Rec*. 2018;183(24):745.
22. Corriveau KM, Giuffrida MA, Mayhew PD, Runge JJ. Outcome of laparoscopic ovariectomy and laparoscopic-assisted ovariohysterectomy in dogs: 278 cases (2003-2013). *J Am Vet Med Assoc*. 2017;251(4):443-450.
23. de Bleser B, Brodbelt DC, Gregory NG, Martinez TA. The association between acquired urinary sphincter mechanism incompetence in bitches and early spaying: a case-control study. *Vet J*. 2011;187(1):42-47.
24. Blendinger C, Blendinger K, Bostedt H. [Urinary incontinence in spayed bitches. 1. Pathogenesis, incidence and disposition]. *Tierarztl Prax*. 1995;23(3):291-299.
25. Ruckstuhl B. [Urinary incontinence in bitches as a late consequence of castration]. *Schweiz Arch Tierheilkd*. 1978;120(3):143-148.
26. Reichler IM, Hung E, Dolf G. The effect of prepubertal or postpubertal spaying on the risk of canine urinary incontinence. *Reprod Domest Anim*. 2015;50:68-68.
27. van Goethem B, Schaefers-Okkens A, Kirpensteijn J. Making a rational choice between ovariectomy and ovariohysterectomy in the dog: a discussion of the benefits of either technique. *Vet Surg*. 2006;35(2):136-143.
28. Holt PE. Urinary incontinence in the bitch due to sphincter mechanism incompetence prevalence in referred dogs and retrospective analysis of sixty cases, Journal of Small Animal Practice Volume 26, Issue 4. *J Small Anim Pract*. 1985;26(4):181-190.
29. Hsueh C, Giuffrida M, Mayhew PD, et al. Evaluation of pet owner preferences for operative sterilization techniques in female dogs within the veterinary community. *Vet Surg*. 2018;47(S1):O15-O25.
30. Devitt CM, Cox RE, Hailey JJ. Duration, complications, stress, and pain of open ovariohysterectomy versus a simple method of laparoscopic-assisted ovariohysterectomy in dogs. *J Am Vet Med Assoc*. 2005;227(6):921-927.
31. Davidson EB, Moll HD, Payton ME. Comparison of laparoscopic ovariohysterectomy and ovariohysterectomy in dogs. *Vet Surg*. 2004;33(1):62-69.
32. Hancock RB, Lanz OI, Waldron DR, Duncan RB, Broadstone RV, Hendrix PK. Comparison of postoperative pain after ovariohysterectomy by harmonic scalpel-assisted laparoscopy compared with median celiotomy and ligation in dogs. *Vet Surg*. 2005;34(3):273-282.
33. Culp WT, Mayhew PD, Brown DC. The effect of laparoscopic versus open ovariectomy on postsurgical activity in small dogs. *Vet Surg*. 2009;38(7):811-817.
34. Nickel R, Sturzbecher N, Kilian H, Arndt G, Brunnberg L. Postoperative convalescence after laparoscopic and conventional ovariectomy: a comparative study. *Kleintierpraxis*. 2007;52(7):413-424.
35. Laflamme D. Development and validation of a body condition score system for dogs. *Canine Practice*. 1997;22(4):10-15.
36. Byron JK, March PA, Chew DJ, DiBartola SP. Effect of phenylpropanolamine and pseudoephedrine on the urethral pressure profile and continence scores of incontinent female dogs. *J Vet Intern Med*. 2007;21(1):47-53.
37. Byron JK, Chew DJ, McLoughlin ML. Retrospective evaluation of urethral bovine cross-linked collagen implantation for treatment of urinary incontinence in female dogs. *J Vet Intern Med*. 2011;25(5):980-984.
38. Scott L, Leddy M, Bernay F, Davot JL. Evaluation of phenylpropanolamine in the treatment of urethral sphincter mechanism incompetence in the bitch. *J Small Anim Pract*. 2002;43(11):493-496.

39. Luettmann K, Merle R, Nickel R. Retrospective analysis after endoscopic urethral injections of glutaraldehyde-cross-linked-collagen or dextranomer/hyaluronic acid copolymer in bitches with urinary incontinence. *J Small Anim Pract*. 2019;60(2):96-101.
40. Reichler IM, Hubler M, Jochle W, Trigg TE, Piche CA, Arnold S. The effect of GnRH analogs on urinary incontinence after ablation of the ovaries in dogs. *Theriogenology*. 2003;60(7):1207-1216.
41. Coit VA, Gibson IF, Evans NP, Dowell FJ. Neutering affects urinary bladder function by different mechanisms in male and female dogs. *Eur J Pharmacol*. 2008;584(1):153-158.
42. Ponglowhapan S, Church DB, Khalid M. Differences in the proportion of collagen and muscle in the canine lower urinary tract with regard to gonadal status and gender. *Theriogenology*. 2008;70(9):1516-1524.
43. Ponglowhapan S, Church DB, Khalid M. Effect of the gonadal status and the gender on glycosaminoglycans profile in the lower urinary tract of dogs. *Theriogenology*. 2011;76(7):1284-1292.
44. Ponglowhapan S, Church DB, Khalid M. Expression of prostaglandin E(2) receptor subtypes in the canine lower urinary tract varies according to the gonadal status and gender. *Theriogenology*. 2010;74(8):1450-1466.
45. Ponglowhapan S, Church DB, Khalid M. Expression of cyclooxygenase-2 in the canine lower urinary tract with regard to the effects of gonadal status and gender. *Theriogenology*. 2009;71(8):1276-1288.
46. Coit VA, Dowell FJ, Evans NP. Neutering affects mRNA expression levels for the LH- and GnRH-receptors in the canine urinary bladder. *Theriogenology*. 2009;71(2):239-247.
47. Olson PN, Mulnix JA, Nett TM. Concentrations of luteinizing hormone and follicle-stimulating hormone in the serum of sexually intact and neutered dogs. *Am J Vet Res*. 1992;53(5):762-766.
48. Ponglowhapan S, Church DB, Khalid M. Differences in the expression of luteinizing hormone and follicle-stimulating hormone receptors in the lower urinary tract between intact and gonadectomised male and female dogs. *Domest Anim Endocrinol*. 2008;34(4):339-351.
49. Reichler IM, Welle M, Sattler U, et al. Comparative quantitative assessment of GnRH- and LH-receptor mRNA expression in the urinary tract of sexually intact and spayed female dogs. *Theriogenology*. 2007;67(6):1134-1142.
50. Arlt S, Wehrend A, Reichler IM. [Neutering of female dogs - old and new insights into Pros and Cons]. *Tierarztl Prax Ausg K Kleintiere Heimtiere*. 2017;45(4):253-263.
51. Nickel R. *Studies on the function of the urethra and bladder in continent and incontinent female dogs* [PhD thesis]. Utrecht: PhD Thesis, University Press; 1998.
52. Eichelberg H, Seine R. [Life expectancy and cause of death in dogs. I. The situation in mixed breeds and various dog breeds]. *Berl Munch Tierarztl Wochenschr*. 1996;109(8):292-303.
53. Inoue M, Kwan NCL, Sugiura K. Estimating the life expectancy of companion dogs in Japan using pet cemetery data. *J Vet Med Sci*. 2018;80(7):1153-1158.
54. Lewis TW, Wiles BM, Llewellyn-Zaidi AM, Evans KM, O'Neill DG. Longevity and mortality in Kennel Club registered dog breeds in the UK in 2014. *Canine Genet Epidemiol*. 2018;5:10.
55. Proschowsky HF, Rugbjerg H, Ersboll AK. Mortality of purebred and mixed-breed dogs in Denmark. *Prev Vet Med*. 2003;58(1-2):63-74.
56. Holt PE. *Studies on the control of urinary incontinence in the bitch*. [PhD]. Bristol, University of Bristol; 1987.
57. Belanger JM, Bellumori TP, Bannasch DL, Famula TR, Oberbauer AM. Correlation of neuter status and expression of heritable disorders. *Canine Genet Epidemiol*. 2017;4:6.

58. Kustritz MVR. Effects of Surgical Sterilization on Canine and Feline Health and on Society. *Reprod Domest Anim*. 2012;47:214-222.
59. Reichler IM. Gonadectomy in cats and dogs: a review of risks and benefits. *Reprod Domest Anim*. 2009;44 Suppl 2:29-35.
60. Howe LM. Current perspectives on the optimal age to spay/castrate dogs and cats. *Vet med (Auckland, NZ)*. 2015;6:171-180.

Table 1: Comparison of the characteristics and observation period of matched paired dogs (n=308) spayed by laparoscopy or laparotomy. The mean values with standard deviations are given for each group, and the 95% confidence intervals (95% CIs) for the differences of the means obtained by paired t-tests are given.

	Laparoscopy	Laparotomy	95% CI
Bodyweight (kg)	27.4±10.2	26.6±11.2	-0.37 to 1.95
Body condition score (BCS) (9 point scale)	4.7±1.0	4.7±1.0	-0.17 to 0.27
Age at spaying (years)	1.6±1.3	1.7±1.5	-0.24 to 0.01
Time interval since spaying (years)	8.6±2.7	8.7±2.4	-0.64 to 0.33
Observed age (years)	10.1±2.8	10.4±2.8	-0.77 to 0.22

Table 2: Conditional logistic regression analyses of 154 matched pairs of dogs in regard to the risk for acquired urinary incontinence (AUI). Each pair consisted of a dog spayed by the laparoscopic approach and a dog spayed by the laparotomic approach. The continuous variables included were bodyweight, body condition score (BCS) at the time of the questionnaire, age at spaying and time interval since spaying (conditional regression analysis a) or observed age (conditional regression analysis b). The dogs were matched for these variables as well as for breed and for time of spaying with regard to the onset of puberty. The 95% confidence intervals (95% CIs) are given, and p-values below 0.05 were considered significant.

	Variables	95% CI		p-value
a)	Surgical approach	0.50	2.27	0.861
	Bodyweight	0.84	1.08	0.436
	BCS	0.78	2.18	0.298
	Age at spaying	0.46	4.62	0.513
	Time interval since spaying	1.03	1.94	0.031
b)	Surgical approach	0.50	2.27	0.861
	Bodyweight	0.84	1.08	0.436
	BCS	0.78	2.18	0.298
	Age at spaying	0.32	3.36	0.948
	Observed age	1.03	1.94	0.030

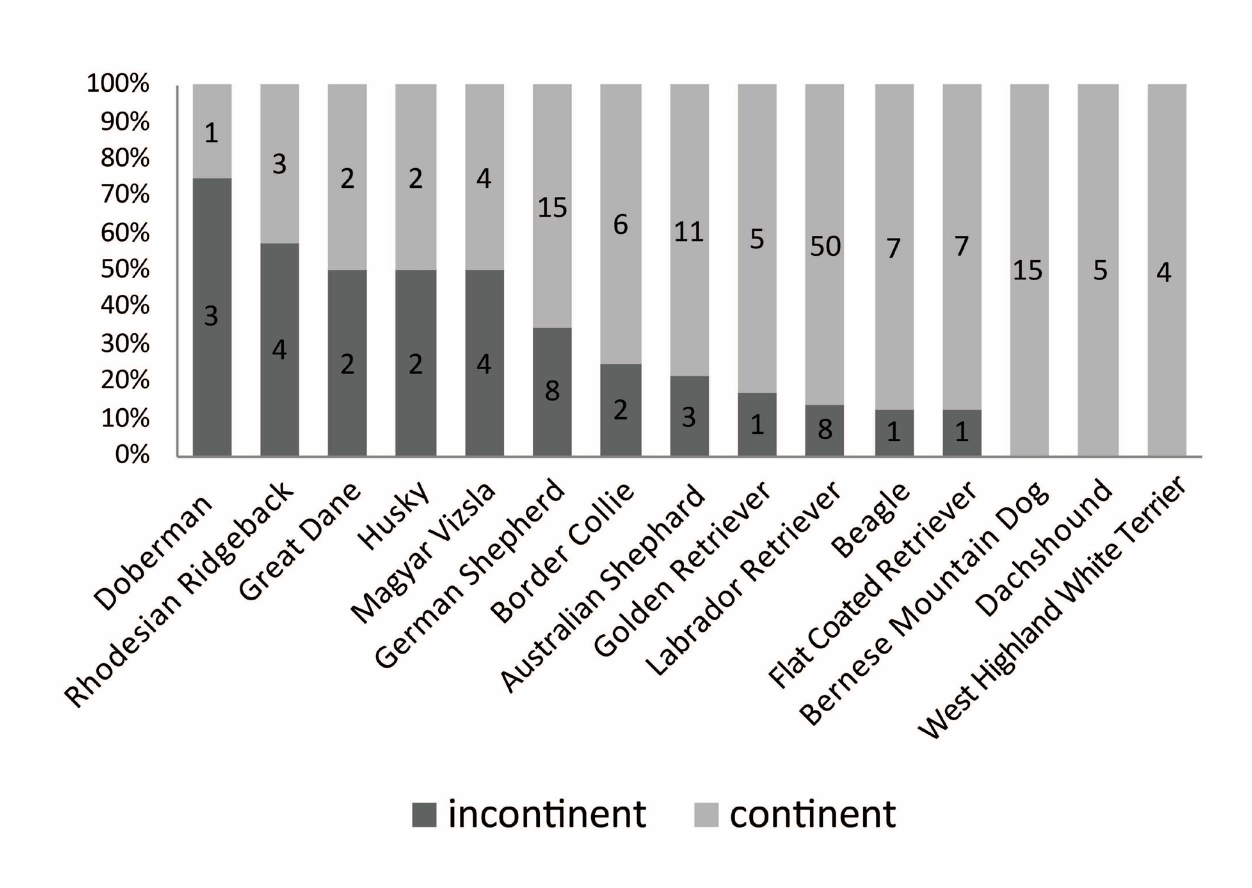

Figure 1: The most common breeds in order of prevalence of acquired urinary incontinence out of a population of 308 matched paired spayed dogs. Only purebred dogs with 4 or more representatives are shown.

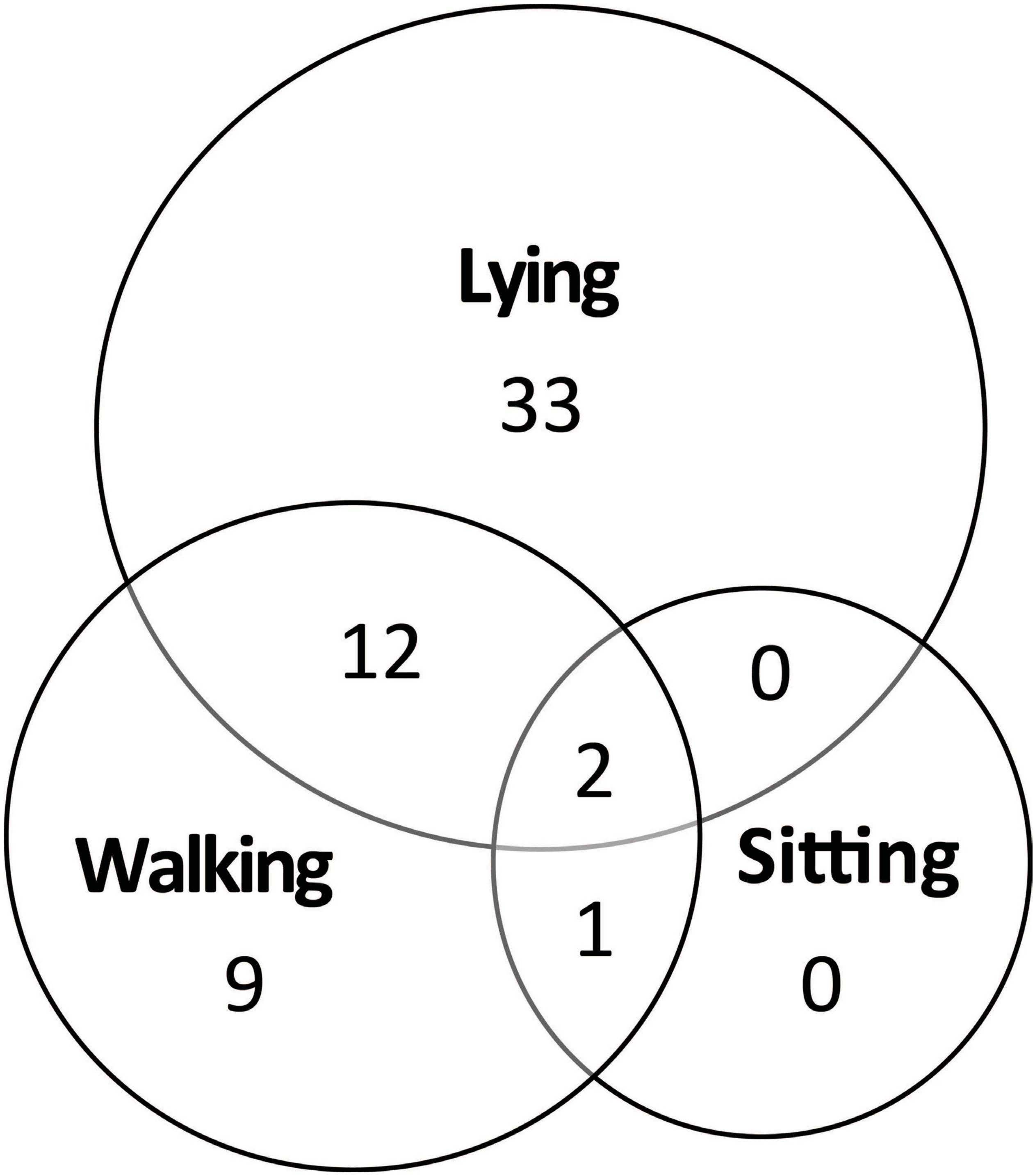

Figure 2: The body position of 57 dogs when acquired urinary incontinence was observed by the owner. In two dogs, information about the body position during urine loss was not available.

Supplemental material

Supporting Information Table. Characteristics and results of previous studies investigating the frequency of acquired urinary incontinence after spaying.

Study	Inclusion criteria	Case identification	Study type	Time interval since spaying	Bodyweight	Number of dogs	Cases
Binder et al., 2018	Minimum follow-up period of 12 months	Owner questionnaire (email)	Retrospective cohort study	1 to 8 years	n.g.	65	10
Corriveau et al., 2017	Spayed laparoscopically between 2003-2013 Dogs with preoperative urinary tract abnormalities included Long-term follow-up (> 14 days after surgery)	Owner questionnaire (email, phone)	Retrospective cohort study	7.6 years	n.g.	207	19
O'Neill et al., 2017	Dogs with electronic patient records	Case records with veterinary diagnosis of AUI/prescription of Phenylpropanolamine/estradiol	Retrospective cohort study	n.g.	Median: 22.6kg	Spayed: 35631	594
						Intact: 8648	30
Brinkmann, 2015	Owner of legal age	Online owner questionnaire	Retrospective cohort study	n.g.	n.g.	Surgical or chemical spaying: 2051	230
					n.g.	Intact: 1471	17
Forsee et al., 2013	Dogs spayed 1-6 years ago	Owner questionnaire (written, email, phone)	Cross sectional	4 to 7 years	n.g.	Spayed: 566	29
Veronesi et al., 2009	Dogs spayed ≤10 years ago	Clinical exam	Cross sectional	Up to 10 years	n.g.	Spayed: 750	38
Reichler et al., 2005	>1 year of age, ≥2 kg, no inborn incontinence	Dog shows, clinical exam	Retrospective cohort study	Mean: 3.5 years	Spayed: median: 21.3kg	Spayed: 310	64
					Intact: median: 21.0kg	Intact: 195	4
Spain et al., 2004	Spayed dogs between 6 weeks and 12 months of age	Owner questionnaire	Retrospective cohort study	Median 4.5 years	n.g.	Spayed: 1659	Spayed <3 months of age: 12.9%
					n.g.		Spayed 3-12 months of age: 5%
Angioletti et al., 2004	Spayed dogs	Clinical exam, ruling out other incontinence etiologies	Prospective cohort study, follow-up every 3 months	Up to 6 years	n.g.	Spayed: 430	22
Stöcklin-Gautschi, 2000	Spayed before puberty, at least 3 years ago	Owner questionnaire, AUI occurred after spaying	Retrospective cohort study	Mean: 5.9 years	n.g.	Spayed: 206	20
					n.g.	Intact: 78	0
Thrusfield et al., 1998	Continent puppy at age of 12 weeks	Owner questionnaire by phone	Retrospective cohort study	245 spayed dogs: ≥ 5 years, 101 spayed dogs: 0.67-4.83 years	n.g	Spayed: 346	18
					n.g.	Intact: 395	4
Okkens et al., 1997	Dogs spayed 8-11 years ago	Owner questionnaire (written, phone)	Cross sectional study	n.g.	Median: 22kg range: 1.6-37.5kg	Spayed: 135	15
Holt and Thrusfield, 1993	Dogs with hormonal UI between 1971-1991 Control animals >1 year of age	Case records with AUI responding to hormonal therapy	Cross sectional study	n.g.	n.g.	Spayed: 1734	53
					n.g.	Intact: 5325	10
Arnold et al., 1989	Dogs spayed 3-10 years ago	Owner questionnaire	Cross sectional study	Range: 3-10 years	n.g.	Spayed: 412	83
Krawiec, 1989	Dogs seen in hospital between 1981-1986	Case records with all type of UI	Cohort study	n.g.	n.g.	Spayed: 3136	73
					n.g.	Intact:4126	8
Thrusfield, 1985	Dogs spayed > 6 months of age	Case records with AUI responding to estrogen therapy	Cohort study	n.g.	n.g.	Spayed: 791	34

Danksagung

Mein besonderer Dank gilt Frau Prof. Dr. Iris M. Reichler - meiner Doktormutter. Für die außerordentliche Betreuung und Unterstützung während der gesamten Zeit meiner Dissertation bin ich ihr unendlich dankbar. Ohne sie und unser gemeinsames Durchhaltevermögen wäre diese Arbeit nicht entstanden. Ich werde unsere gemeinsame Zeit vermissen.

Vielen herzlichen Dank an Dr. Sonja Hartnack für die statistischen Auswertungen und die Unterstützung in statistischen Fragen.

Ein großes Dankeschön auch an Orsolya Balogh und Pentti Timonen für die Hilfe bei Formulierungen.

Ich danke außerdem dem gesamten Team der Kleintierreproduktion, dass sie mich vom ersten Tag an so herzlich in ihr Team aufgenommen haben. Ich werde die Zeit am Tierspital vermissen.

Den Hundebesitzern, die sich auf das Interview eingelassen und mir geduldig meine Fragen beantwortet haben, gilt ebenfalls besonderer Dank. Außerdem danke ich herzlich den Tierkliniken, die mir ihre Daten zu Verfügung gestellt haben.

Zu guter Letzt möchte ich mich bei meinen Eltern bedanken, die mir sowohl mein Studium, als auch meine Dissertation überhaupt erst ermöglicht haben, mich stets unterstützen und immer für mich da sind.

Curriculum Vitae

Vorname Name	Katharina-Marie Lutz
Geburtsdatum	07.02.1992
Geburtsort	München
Nationalität	Deutsch

	Schulausbildung
09/1998 – 08/2002	Grundschule Aschheim, Aschheim, Deutschland
09/2002 – 05/2011	Gymnasium Kirchheim, Kirchheim b. München, Deutschland
	Höchster Schulabschluss
02.05.2011	Abitur, Gymnasium Kirchheim, Kirchheim b. München, Deutschland
	Studium
09/2011 - 09/2013	Veterinärmedizin, Veterinärmedizinische Universität Budapest, Budapest, Ungarn
10/2013 - 03/2017	Veterinärmedizin, Freie Universität Berlin, Berlin, Deutschland
	Abschlussprüfung vet. med.
16.02.2017	Freie Universität Berlin, Berlin, Deutschland
	Anfertigung der Dissertation
08/2017 – 07/2019	unter Leitung von Prof. Dr. med. vet. Iris Margaret Reichler
	am Departement für Nutztiere, Klinik für Reproduktionsmedizin, Abteilung für Kleintierreproduktion der Vetsuisse-Fakultät Universität Zürich
	Direktor Prof. Dr. med. vet. Heiner Bollwein
	Alle fachrelevanten Anstellungen nach Abschluss des veterinärmedizinischen Studiums
12/2017 – 02/2018	Assistenzärztin, Eurotier-Klinik, El Arenal, Mallorca
12/2017 – 02/2018	Assistenzärztin, Clinica Veterinaria Metropólitan, Palma, Mallorca
10/2018 – 07/2019	Assistenzärztin/Doktorandin, Abteilung für Kleintierreproduktion, Klinik für Reproduktionsmedizin, Departement für Nutztiere, Vetsuisse Fakultät Universität Zürich, Zürich, Schweiz
09/2019 – heute	Assistenzärztin, Tierklinik Weilheim, Weilheim i.OB, Deutschland